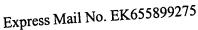
## Express Mail No. EK655899275

## We claim:

TOTAL TENT

- 1. A method for inhibiting metastatic tumors in a mammal suffering from one or more metastatic tumors, said method comprising administering to the mammal a therapeutically effective amount of a DNA sequence comprising a constitutive promoter operatively linked to a transcription sequence; wherein the transcription sequence, when transcribed, produces a messenger RNA sequence that comprises a translatable sequence encoding a toxin, and an untranslated sequence; wherein the untranslated sequence inhibits translation of the toxin sequence in the absence of eukaryotic initiation factor eIF4E, and wherein the untranslated sequence allows translation of the toxin sequence into a toxin in the presence of eukaryotic initiation factor eIF4E.
  - 2. A method as recited in Claim 1, wherein the untranslated region comprises the 5' untranslated sequence of fibroblast growth factor-2; whereby, in a metastatic tumor cell in which the presence of eukaryotic initiation factor eIF4E allows the translation of the toxin, the toxin is translated to kill the tumor cell; and whereby the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eIF4E typically present in non-tumor cells.
  - 3. A method as recited in Claim 1, wherein the untranslated region comprises the 5' untranslated sequence selected from the group consisting of proto-oncogene *c-myc*, cyclin D1, vascular endothelial growth factor, and ornithine carboxylase; whereby, in a metastatic tumor cell in which the presence of eukaryotic initiation factor eIF4E allows the translation of the toxin, the toxin which the presence of eukaryotic initiation factor eIF4E allows the translation of the toxin, the mammal are is translated to kill the tumor cell; and whereby the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eIF4E typically present in non-tumor cells.



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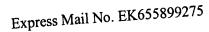
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- 4. A method as recited in Claim 1, wherein the encoded toxin is a conditional toxin.
- thymidine kinase; and wherein the method additionally comprises administering an effective amount of ganciclovir to the mammal; whereby, in ametastatic tumor cell in which the presence of eukaryotic initiation factor eIF4E allows the translation of herpes thymidine kinase, and in which ganciclovir is taken up by the cell, the translated herpes thymidine kinase in the cell phosphorylates the ganciclovir, allowing the phosphorylated ganciclovir to kill the tumor cell; and whereby the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eIF4E typically present in non-tumor cells.
  - 6. A method as recited in Claim 5, wherein the untranslated region comprises the 5' untranslated sequence of fibroblast growth factor-2.
- 7. A method as recited in Claim 5, wherein the untranslated region comprises the 5' untranslated sequence selected from the group consisting of proto-oncogene *c-myc*, vascular endothelial growth factor, and ornithine decarboxylase.
  - 8. A method as recited in Claim 1, wherein the untranslated sequence comprises mRNA
    with a hairpin conformation having a stability of ΔG ≥ 50 Kcal/Mol.





9. A method as recited in Claim 1, wherein the metastatic tumor is associated with a mammalian cancer selected from the group consisting of bladder, breast, cervical, colon, prostate, and head and neck.

10. A DNA sequence for administering to a mammal to inhibiting one or more metastatic tumors, said sequence comprising a constitutive promoter operatively linked to a transcription sequence; wherein the transcription sequence, when transcribed, produces a messenger RNA sequence that comprises a translatable sequence encoding a toxin, and an untranslated sequence; wherein the untranslated sequence inhibits translation of the toxin sequence in the absence of eukaryotic initiation factor eIF4E, and wherein the untranslated sequence allows translation of the toxin sequence into a toxin in the presence of eukaryotic initiation factor eIF4E.

11. A DNA sequence as recited in Claim 10, wherein the untranslated region comprises the 5' untranslated sequence of fibroblast growth factor-2; whereby, in a metastatic tumor cell in which the presence of eukaryotic initiation factor eIF4E allows the translation of the toxin, the toxin is translated to kill the tumor cell; and whereby the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eIF4E typically present in non-tumor cells.

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A DNA sequence as recited in Claim 10, wherein the untranslated region comprises the 5' untranslated sequence selected from the group consisting of proto-oncogene c-myc, vascular endothelial growth factor, and ornithine decarboxylase; whereby, in a metastatic tumor cell in which the presence of eukaryotic initiation factor eIF4E allows the translation of the toxin, the toxin is translated to kill the tumor cell; and whereby the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eIF4E typically present in non-tumor cells..

A DNA sequence as recited in Claim 10, wherein the encoded toxin is a conditional 13. toxin.

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A DNA sequence as recited in Claim 13, wherein the encoded conditional toxin is a herpes thymidine kinase; and wherein the method additionally comprises administering an effective amount of ganciclovir to the mammal; whereby, in a metastatic tumor cell in which the presence of eukaryotic initiation factor eIF4E allows the translation of herpes thymidine kinase, and in which ganciclovir is taken up by the cell, the translated herpes thymidine kinase in the cell phosphorylates the ganciclovir, allowing the phosphorylated ganciclovir to kill the tumor cell; and whereby the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eIF4E typically present in non-tumor cells.

A DNA sequence as recited in Claim 14, wherein the untranslated region comprises 15. 1

the 5' untranslated sequence of fibroblast growth factor-2. 2

- 1
- A DNA sequence as recited in Claim 14, wherein the untranslated region comprises
- the 5' untranslated sequence selected from the group consisting of proto-oncogene c-myc, vascular 2
- endothelial growth factor, and ornithine decarboxylase. 3

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- A DNA sequence as recited in Claim 10, wherein the untranslated sequence comprises 17. mRNA with a hairpin conformation having a stability of  $\Delta G \ge 50$  Kcal/Mol.
  - A DNA sequence as recited in Claim 1, wherein the metastatic tumor is associated with a mammalian cancer selected from the group consisting of bladder, breast, cervical, colon, prostate, and head and neck.

add  $A^3$ )